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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/992,914	12/18/1997	EIJIRO WATANABE	0020-4348P	4405

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EXAMINER	
KRUSE, DAVID H	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/992,914	WATANABE ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004 and 03 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,43 and 46-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 43* is/are allowed.

6)☒ Claim(s) *46-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *28 July 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

STATUS OF THE APPLICATION

Continued Examination Under 37 CFR § 1.114

1. A request for continued examination under 37 CFR § 1.114, including the fee set forth in 37 CFR § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR § 1.114, and the fee set forth in 37 CFR § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR § 1.114. Applicant's submission filed on 15 November 2004 has been entered.

2. This Office action is in response to the Amendments filed 15 November 2004 and 3 December 2004, and the Remarks filed 11 November 2004.

3. Those rejections or objections not specifically addressed in this Office action are withdrawn in view of Applicant's amendments to the claims.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

5. Claims 46-51 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 May 2004. Applicant's arguments filed 15 November 2004 have been fully considered but they are not persuasive.

Applicant argues that the discrepancy in the degree of "homology" in the data set provided by the Applicant and by the Examiner is due to differences in the computer

program used to analyze the data (page 20, 2nd paragraph of the Remarks). This argument is not found to be persuasive because Applicant has failed to adequately describe a structural-functional relationship between the genus of isolated nucleic acids encoding raffinose synthase as broadly claimed and thus establish a substantial utility for the invention of the instant claims.

Applicant argues that BLAST is a local alignment program, and does not make global alignments between sequences to calculate total percent homologies (page 21, 1st paragraph of the Remarks). This argument is not found to be persuasive for the reasons put forth in the previous Office action. Given the evolutionary relationship between raffinose synthase and stachyose synthase, even a local alignment would not adequately distinguish the two simply based on amino acid sequence because both enzymes would have similar binding regions, and distinguishing characteristics are not described in the instant specification.

Applicant argues that the identities between RFSS(raffinose synthase) and STSs (stachyose synthase) are about 40%, and that the identities between RFSS and STSS range from 40% to about 50, the identities among RFSs are 60% or more and that the identities among STSs are also 60% or more. That the identities among RFSs or the identities among STSs are higher than the identities between RFSs and SIPs or the identities between RFSs and STSs, thus, based on the results of analyses by BLAST program, RFSs, SIPs or STSs can be distinguished (pages 21-22 of the Remarks). This argument is not found to be persuasive for the reasons of record.

Applicant argues that identification of a protein by homology analysis as having higher similarity to a Raffinose Synthase than to a Stachyose Synthase or Imbibation Protein is sufficient to establish that protein may be used in the manner similar to that which know Raffinose Synthase proteins may be used (page 23, 1st paragraph of the Remarks). This argument is not found to be persuasive for the reasons given supra.

Claim Rejections - 35 USC § 112

6. Claims 48-77 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 May 2004. Applicant's arguments filed 15 November 2004 have been fully considered but they are not persuasive.

Applicant's arguments as directed to claims 46 and 47, not included in this rejection, are persuasive.

Applicant argues that many of the present claims in fact recite structural features that are plainly set forth in the Sequence Listing and distinguish the generic invention as claimed from other nucleic acids, and also describe functional outcomes (a biological activity of the enzyme) that are associated with those structural features. Applicant further argues that the remaining claims describe the invention in product-by-process terms, and that such a manner of claiming a generic invention is entirely proper (pages 24 and 25 of the Remarks). This argument is not found to be persuasive for the

reasons given in the previous Office actions. Applicant has failed to establish a relationship between the structure of the claimed nucleic acids and the function of the encoded protein. In addition, description of a partial coding sequence does not adequately describe a nucleic acid encoding a raffinose synthase as asserted by Applicant. See *In re Wallach*, 71 USPQ2d 1939 (CA FC 2004), at 1940: Claims in application directed to isolated DNA molecules encoding proteins that inhibit cytotoxic effects of tumor necrosis factor were properly rejected for failure to satisfy written description requirement of 35 U.S.C. § 112, since applicants claimed nucleic acids encoding protein for which they provided only partial sequence, and without approximately 95 percent of amino acid sequence that applicants did not disclose, it cannot be held that DNA molecules claimed in application have been described, since applicants' contention that they were in physical possession of protein does not establish their knowledge of that protein's amino acid sequence or any of its other descriptive properties, even though amino acid sequence is inherent property of protein, and since application does not provide adequate functional description, in that, with only partial amino acid sequence disclosed, chemical structure of nucleic acid molecules that can serve function of encoding protein's amino acid sequence cannot be determined.

7. Claims 46-77 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 2, a chimeric nucleic acid comprising said isolated nucleic acid, a transformant comprising said chimeric nucleic acid, a plasmid comprising said nucleic acid, a host organism either a microorganism or plant comprising said plasmid

and a method of metabolic modification of a plant comprising introducing said isolated nucleic acid, does not reasonably provide enablement for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 4, 6 or 8, or an isolated nucleic acid that hybridizes with a complement to said isolated nucleic acid isolated from any leguminous, lamiaceous or monocotyledonous plant. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 May 2004. Applicant's arguments filed 15 November 2004 have been fully considered but they are not persuasive.

Applicant argues that the Examiner's analysis of the question of undue experimentation looks only at the factor of whether working examples of the claimed invention are described specification and an assertion that it is unpredictable whether any particular nucleic acid produced according the invention would in fact exhibit raffinose to the teachings of synthase activity. Applicant argues that this analysis is legally insufficient to establish *prima facie* lack of enablement, as the Examiner fails to consider the breadth of the claims, the nature of the invention, the level of ordinary skill in the art, the quantity of the experimentation needed, the guidance provided by the specification (other than the presence or absence of working examples) and the state of the art at the time the invention was made (paragraph spanning pages 25-26 of the Remarks). This argument is not found to be persuasive because the Examiner has addressed this issue by addressing not only the breadth of the claimed invention, but also the amount of guidance provided by the specification, the nature of the invention and the level of ordinary skill in the art at the time of Applicant's invention. The issue of

similarity between raffinose synthase and stachyose synthase has been extensively addressed during examination of this application. In the Office action mailed 26 August 2003, the Examiner stated that the art teaches that one of skill in the art cannot assume the function of the polypeptide encoded by an isolated nucleic acid solely based on sequence similarity to a known polypeptide sequence (see Duggleby 1997 and Richmond *et al* 2000, Plant Physiology 124: 495-498, see paragraph spanning left and right column on page 497). In addition, the art teaches that raffinose synthase enzymes have high overall amino acid sequence homology with seed imbibition proteins and stachyose synthases, hence amino acid sequence similarity cannot be used to assert function (see Peterbauer *et al* 2002, Planta 215: 839-846, see page 840, left column and page 841, right column).

Applicant argues that the art of expression of recombinant proteins, is one in which the artisan of ordinary skill expects to perform a few weeks or months of experimentation in generating variants of a protein, then isolating clones encoding those variants and then (perhaps) re-cloning the isolated variants into vectors for expressing a protein, and then screening expressed proteins for activity (page 27, 1st paragraph of the Remarks). This issue is not questioned by the Examiner, what is at issue is whether Applicant has adequately taught one of skill in the art how to make and use the genus of isolated nucleic acids encoding raffinose synthase as broadly claimed. It remains the Examiner's opinion that the instant application is lacking.

Applicant argues that the amount of experimentation needed to practice the present invention is not unduly large or burdensome. Applicant argues that the

practitioner must isolate a template genomic DNA from an organism, perform a polymerase chain reaction using primers described in the specification to generate an amplified fragment, clone that fragment into an expression vector, express the encoded protein and then screen the protein for activity as a raffinose synthase (page 27, 3rd paragraph of the Remarks). This argument is not found to be persuasive because ransom screening of products of isolated nucleic acids is undue trial and error experimentation.

Applicant argues that the raffinose content a number of organisms, especially including plants and some algae, was known and that the biochemistry of raffinose synthesis in plants had been established, and the role of raffinose synthases as rate-limiting of raffinose production was known. Applicant further argues that a biochemical assay for raffinose synthase activity was known in the art (page 28 of the Remarks). This argument is not found to be persuasive because simply having an assay for activity does not mean screening through a myriad of isolated nucleic acids expressed in an organism is not undue trial and error experimentation. For example claim 66 is directed to a plasmid comprising a nucleic acid isolated from any leguminous, lamiaceous or monocotyledonous plant, wherein Applicant has only taught how to make and use a nucleic acid from broad bean encoding the amino acid sequence of SEQ ID NO: 2. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a

single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.".

Applicant argues that the specification provides details such as organisms likely to be useful for isolating template genomic DNA or cDNA (see, e.g. page lines 9-14) and methods for cloning DNA encoding a putative raffinose synthase enzyme from an RNA fraction. Applicant argues that the specification describes methods for expressing the cloned DNA in plant cells and in bacteria. Applicant argues that the specification describes how to purify raffinose synthase from plant cells and a biochemical assay for raffinose synthase. Applicant argues that the specification provides a number of working examples of isolation of partial or complete raffinose synthase genes from a number of plants (page 29 of the Remarks). These arguments are not found to be persuasive because Applicant provides evidence of the function of the encoded product of a single nucleic acid, the function of the encoded product of other nucleic acids taught is only speculative and not supported by the teachings of the specification.

Applicant argues that the skilled artisan can follow detailed teachings in the specification of how to clone, express and evaluate DNAS that are likely to encode functional raffinose synthase enzymes. Applicant argues that it is very likely that the skilled artisan would find a cloned DNA encoding a functional enzyme by following the teachings of the specification (page 30, 2nd paragraph of the Remarks). These

arguments are not found to be persuasive because Applicant is only teaching methods of experimentation, not how to make and use nucleic acids encoding raffinose synthase as broadly claimed.

Applicant argues that the *Wands* case supports the arguments put forth (paragraph spanning pages 30-31 of the Remarks). This is not found to be persuasive because in the case of *in re Wands*, all of the starting materials were know in the art at the time of the invention, and one of skill in the art would know the structure of the produced IgM antibodies and could distinguish them from other antibodies, and would know how to use such IgM antibodies. In the instant case, one of skill in the art would not know how to make and use the genus of nucleic acids encoding raffinose synthase as broadly claimed by Applicant without undue trial and error experimentation.

Double Patenting

8. Claims 46, 47, 52, 53, 55 and 59-77 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 16-23 and 28-30 of copending Application No. 09/301,766. This rejection is repeated for the reason of record as set forth in the last Office action mailed 14 May 2004. Applicant's arguments filed 15 November 2004 have been fully considered but they are not persuasive.

Applicants requests that the Examiner hold this rejection in abeyance until either this application or the '766 application is allowed, at which time an appropriate response in the form either arguments distinguishing the invention or a terminal disclaimer will be filed in the application that remains under examination. The rejection is herein

maintained. The instant Application teaches an isolated nucleic acid isolated from soybean asserted as encoding a raffinose synthase. The copending Application teaches an isolated nucleic acid isolated from soybean, which is a partial sequence, which is asserted as encoding a raffinose synthase.

Conclusion

9. Claims 6 and 43 are allowed.

10. Claims 46-77 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.

DAVID H. KRUSE, PH.D.
PRIMARY EXAMINER

David H. Kruse, Ph.D.
7 March 2005

12. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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